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EDITORIAL · REDAKSIONEEL

A NEW BLOOD FACTOR

DISCOVERED IN SOUTH AFRICA

In a recent issue of the *Journal of Forensic Medicine* (Volume 7, No. 2, 1960), Dr. Maurice Shapiro (Medical Director of the South African Blood Transfusion Service, Johannesburg) reports the discovery (in the blood of Mrs. Shabalala, the mother of an erythroblastotic baby) of a new blood group antibody in the Rh-Hr system. The blood factor identified by this antibody he has designated **hr**^{S} (the Shabalala factor).

Shapiro has shown that most so-called anti-**hr**″ sera (designated as anti-e in the Fisher-Race terminology) contain 2 antibodies, viz. anti-**hr**″ and anti-**hr**^{S}. These 2 antibodies are virtually identical in their serological reactions, except that certain bloods which contain **hr**″ fail to react with anti-Shabalala antibody. Such bloods are rare in Whites but are fairly common in the South African Bantu.

The discovery is of great importance in the forensic application of blood grouping tests for disputed parentage. Hitherto the Committee on Medico-Legal Problems of the American Medical Association has wisely cautioned against the use of anti-**hr**″ sera because there have been several anomalous findings. For example, in a case where there was no biological doubt about the relationship,

'N NUWE BLOEDFAKTOR

ONTDEK IN SUID-AFRIKA

In 'n onlangse uitgawe van die *Journal of Forensic Medicine* (Deel 7, No. 2, 1960) doen dr. Maurice Shapiro (Mediese Direkteur van die Suid-Afrikaanse Bloedoortappingsdiens, Johannesburg) verslag oor die ontdekking (in die bloed van mev. Shabalala, die moeder van 'n eritroblastotiese babetjie) van 'n nuwe bloedgroepteenstof in die Rh-Hr-stelsel. Hy noem die bloedfaktor wat deur hierdie teenstof geïdentifiseer is, **hr**^{S} (die Shabalala-faktor).

Shapiro het aangetoon dat die meeste sogenaamde anti-**hr**″-serums (aangedui as anti-e in die Fisher-Race-terminologie) 2 teenstowwe bevat, nl. anti-**hr**″ en anti-**hr**^{S}. Hierdie 2 teenstowwe is feitlik identiek wat hul serologiese reaksies betref, behalwe dat sekere bloedsoorte wat **hr**″ bevat nie met die anti-Shabalala-teenstof reageer nie. Sulke bloedsoorte is 'n seldsaamheid by blankes, maar 'n betreklik gewone verskynsel by die Suid-Afrikaanse Bantoe.

Die ontdekking is van groot belang in die geregtelik-geneeskundige toepassing van bloedgroeptoetse in gevalle waar die ouerskap van 'n kind betwis word. Die Komitee insake Medies-geregtelike Probleme van die Amerikaanse Mediese Vereniging het tot dusver 'n verstandige woord van waarskuwing laat hoor teen die gebruik van anti-**hr**″-serums omdat

a mother (type Rh_0) was apparently excluded as the parent of her own child (typed as Rh_2Rh_2 by a negative reaction with anti-**hr″** serum). The explanation of this and similar anomalies can now be understood in the light of the discovery of the Shabalala factor, the reason being that the test sera used in these investigations contained only anti-Shabalala antibody and no anti-**hr″**.

The Shabalala discovery makes possible for the first time the selection of sera which contain an adequate titre of the specific anti-**hr″** antibody and thus also makes possible the confident use of such sera in medico-legal investigations.

Apart from its practical applications, the genetic implications are far-reaching. The observations cannot be explained in terms of the Fisher-Race theory of inheritance of the Rh blood groups. This postulates:

(*a*) A 1:1 correspondence between antigen, antibody and gene.

(*b*) Three closely linked genes on the chromosome determining the entire Rh-Hr pattern.

(*c*) That the genes which can be accommodated at the individual loci are alleles and reciprocally related to one another, e.g. *D-d; C-C*^{W}*-c; E-e.*

The Shabalala and **hr″** factors, though closely associated are not alleles (since both are usually present); nor are they reciprocally related. An additional locus would therefore have to be allocated to the new factor. Similarly, the additional loci required to accommodate several other blood factors such as **rh**$_i$, **hr**^{V}, **hr** and the series of blood factors associated with **Rh**$_1$ (i.e. **Rh**^{A}, **Rh**^{B} . . . etc. the first example of which was also reported by Shapiro *); and the prospect of new discoveries which will extend the number of independent loci indefinitely, all challenge the Fisher-Race theory of 3 closely linked genes, so closely linked that they behave almost invariably as a single unit in meiosis.

On the other hand, the Shabalala findings support Wiener's contention that the Rh blood groups are inherited by a series of allelic genes, each of which determines the transmission of a complex of blood factors as a unit. This unit represents all the blood factors contained in the particular agglutinogen. Wiener's theory places no arbitrary limits on the number of potential blood factors which may be represented in the agglutinogen nor does it attempt to anticipate their serological properties. While new discoveries have necessitated daar etlike afwykende bevindings was. By-voorbeeld, in 'n geval waar daar hoegenaamd geen biologiese twyfel oor die verwantskap bestaan het nie is 'n moeder (tipe Rh_0) skynbaar uitgesluit as die moeder van haar eie kind (getipeer as Rh_2Rh_2 deur 'n negatiewe reaksie met anti-**hr″**-serum). Die verduideliking van hierdie en dergelike anomalieë kan nou begryp word in die lig van die ontdekking van die Shabalala-faktor. Die rede is dat die toetsserums wat vir hierdie ondersoeke gebruik is, slegs die anti-Shabalala-teenstof bevat het, en geen anti-**hr″** nie.

Die Shabalala-ontdekking maak dit nou vir die eerste keer moontlik om serums te kies wat 'n voldoende titer van die spesifieke anti-**hr″**-teenstof bevat, en maak dit dus ook moontlik om sodanige serums met vertroue vir medies-geregtelike ondersoekwerk te gebruik.

Afgesien van die praktiese toepassings is die genetiese implikasies verreikend. Die waarnemings kan nie verduidelik word op grond van die Fisher-Race-teorie van erflikheid van die Rh-bloedgroepe nie. Hierdie teorie postuleer:

(*a*) 'n 1 : 1-ooreenstemming tussen antigeen, teenstof en geen.

(*b*) Drie ten nouste verwante gene op die chromosoom wat die hele Rh-Hr-patroon bepaal.

(*c*) Dat die gene wat by die individuele loci geakkommodeer kan word, allelomorfe en wederkerig verwant aan mekaar is, bv. D-d; C-C^{w}-c; E-e.

Die Shabalala- en **hr″**-faktore, hoewel hulle geassosieer is, is nie allelomorfe nie (aangesien albei gewoonlik aanwesig is); nòg is hulle wederkerig verwant. 'n Addisionele locus sal derhalwe aan die nuwe faktor toegeken moet word. Insgelyks, die addisionele loci wat nodig is vir die akkommodasie van etlike ander bloedfaktore soos **rh**$_i$, **hr**^{V}, **hr** en die reeks bloedfaktore geassosieer met **Rh**$_0$ (d.w.s. **Rh**^{A}, **Rh**^{B} . . . ens., die eerste voorbeeld waarvan ook deur Shapiro* gerapporteer is); en die vooruitsig op nuwe ontdekkings wat die aantal onafhanklike loci onbepaald kan uitbrei, is almal 'n uitdaging van die Fisher-Race-teorie van 3 gene wat ten nouste verwant is, so nou, trouens, dat hulle byna altyd as 'n enkele eenheid in meiose optree.

Aan die ander kant steun die Shabalala-bevindings Wiener se bewering dat die Rh-bloedgroepe geërf word deur 'n reeks allelomorfiese gene, iedereen waarvan die oordrag van 'n kompleks van bloedfaktore as 'n eenheid bepaal. Hierdie eenheid verteenwoordig al die bloedfaktore vervat in die besondere agglutinogeen. Wiener se teorie stel geen arbitrêre perke aan die aantal potensiële bloedfaktore wat

* Shapiro, M. (1951): S. Afr. Med. J., **25**, 191.

* Shapiro, M. (1951): S. Afr. Tydskr. Geneesk., **25**, 191.

sitated certain modifications in Wiener's notations from time to time, his theory has required no amendment or qualification since it was first put forward on the evidence available in 1942.

The elucidation of the serology and genetics of the Shabalala factor represents a major advance in the field of human blood grouping. It is a fitting tribute to South African medical science that its discoverer has been invited to participate in a special seminar organized by the American Association of Blood Banks to commemorate the 60th anniversary of the discovery of the ABO blood groups by Karl Landsteiner.

in die agglutinogeen verteenwordig kan wees nie, en dit wend ook geen poging aan om hul serologiese eienskappe vooruit te bepaal nie. Terwyl nuwe ontdekkings dit van tyd tot tyd noodsaaklik gemaak het om sekere wysigings in Wiener se aantekeninge aan te bring, het sy teorie geen wysiging of kwalifikasie geverg sedert dit in 1942, op grond van die bewyse wat destyds beskikbaar was, aan die hand gedoen is nie.

Die verduideliking van die serologie en genetika van die Shabalala-faktor kan as 'n belangrike vordering op die gebied van die groepering van menslike bloed beskou word. Dit is 'n passende huldeblyk aan Suid-Afrika se mediese wetenskap dat die ontdekker daarvan uitgenooi is om lid te word van die spesiale studiegroep wat deur die Amerikaanse Vereniging van Bloedbanke georganiseer is om die 60ste jaardag van die ontdekking van die ABO-bloedgroepe deur Karl Landsteiner te herdenk.

ABSTRACTS

THE EARLY DIAGNOSIS OF PREGNANCY

The authors examined at frequent intervals the urine of a woman who had been artificially inseminated and whose subsequent pregnancy ran a normal course. They were thus afforded the rare opportunity of checking the reliability of certain pregnancy tests at various known times.

On the sixth day following nidation, i.e. 2 days before the estimated date for the commencement of the next menses, the forced rabbit reaction (in which the rabbit is injected with the alcoholic extract of 50 c.c. urine) yielded positive results. The Reiprich-Salmon test (hyperaemia of the rat ovary, 5 c.c. urine) was not positive until another 5 days had elapsed. The Friedmann test (rabbit ovary, 10 c.c. urine) was positive after a further 2 days. On the other hand, the tests with *male* amphibia (frog, toad) did not provide reliable results until 17 days after nidation.

Hormone determinations showed that prolan B begins to be secreted almost immediately after implantation of the ovum. Thus, some 5 rabbit units per litre of urine were measured on the third day after implantation, about 20 on the sixth day, about 50 on the eleventh day, about 100 on the 13th day and about 200 on the 17th day.

[Hinglais, H. and Hinglais, M. (1959): Sem. Thérap., **35**, 344].

CLINICAL TRIALS WITH NEW CORTICOSTEROIDS

The authors used dexamethasone in the treatment of 100 patients and were able in most cases to compare the results with those of previous therapy with prednisone, prednisolone or methylprednisolone.

A good or very good response was elicited in 32 of 39 patients with rheumatoid arthritis, dexamethasone being superior to the other hormones in 21 cases and inferior in only 3. Rheumatic fever responded approximately equally well to all the hormones. In cases of gout, dexamethasone was less effective. The daily doses in articular diseases were 1–3.5 mg. The potency ratio was on the average 7 : 1, sometimes as much as 10 : 1, i.e. the effect was 7 or 10 times greater than with other hormones. Allergic diseases (bronchial asthma, allergic skin conditions) could often be brought under control with daily doses of as little as 1–1.5 mg. dexamethasone, sometimes with even 0.2–0.5 mg. The results were beneficial in 21 of 29 patients. The potency ratio was 10 : 1, even more in some cases. Dexamethasone was superior to the other hormones in 17 cases, and never inferior. Dexamethasone regularly exerted a beneficial effect in Addison's disease or hypopituitarism. The potency ratio here was 10–15 : 1, a daily dose of 0.5 mg. frequently sufficing in adrenocortical insufficiency. Dexamethasone displayed a particularly pronounced effect in the adrenogenital syndrome, for here it proved 40 or 56 times more potent than methylprednisolone.

[Lichtwitz, A., Hioco, D. and Greslé, C. (1959): Sem. Hôp. Paris, **35**, 1570].

ANTI-POLIOMYELITIS VACCINATION

Sabin explains the reasons in favour of immunization against poliomyelitis with attenuated, live virus vaccines. A vaccine of this type is probably better able than formalinized vaccines to eliminate the possibility of paralytic poliomyelitis. Unlike the formalinized vaccine, the vaccine containing attenuated pathogens can also be used to check a threatened epidemic or one that has already begun. The formalinized vaccine presumably acts by raising the titre of circulating antibodies which block the passage of the virus from the digestive tract to the CNS. It does not, however, prevent the intestinal tract from being infected by the virus, whereas the Sabin vaccine does. It is supposed that this effect sets in very rapidly and that virulent strains are thus rendered safe within a short time.

Admittedly, the attenuated vaccine may change its properties during its passage through the human intestine, the neurotropism of the virus appearing in some cases to increase a little. Possibly, however, the highly attenuated strains of polioviruses used by Sabin (which only damage lower motor neurones when they are injected into the spinal cord in the immediate vicinity of these neurones) have finally lost their harmful effect on the CNS, although this is difficult to prove. The tests carried out so far have yielded encouraging results, but the genetic behaviour of the poliovirus has not yet been fully investigated.

[Sabin, A. B. (1959): Brit. Med. J., **1**, 663].

CORNEAL HETEROGRAFTS

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'L' idée de Reisinger qui consiste a remplacer la cornée trouble d' un homme par la cornée claire d' un animal est, une faintaisie audacieuse et serait le plus grand succès de la chirurgie ci cette operation réussissait.' *Diffenbach,* 1830.[1]

A pressing problem in corneal grafting is the shortage of human donor corneas. While it is difficult enough to obtain corneal material for operations of election, the supply position breaks down completely in the case of corneal grafting under emergency conditions. Most surgeons will not use corneas which have been preserved for much longer than 48 hours by current techniques.

A great advance in this field has been made by Professor Payrau, of Paris, who devised 2 techniques for processing corneas so that they can be used after long months of storage at room temperature.[2, 3] Payrau found that, when bovine or canine corneas were rapidly frozen at very low temperatures and then desiccated, they were altered in some way which allowed them to be grafted successfully into human eyes. He has performed numbers of heterografts of this kind in which the donor cornea has remained perfectly transparent. His technique succeeded with lamellar grafts, but not with penetrating grafts.

In the present study, the author grafted bovine corneas into 2 human eyes after the former had been stored for several months. The corneas were prepared in France by the Institute Chibret, according to Payrau's technique, some time before September 1959. The desiccated, sterile corneas were attached to plastic supports inside air-tight containers. They were posted to South Africa where they were stored at room temperature in Johannesburg during a typical summer. The first cornea was used on 19 October 1959 and the second on 18 January 1960. At operation, the containers were opened and the corneas, still attached to their plastic supports, were dipped in normal saline for about 10 minutes. Lamellar grafts were then cut in the usual way.[4]

Case 1. A female aged about 50 had a recurrent type of pterygium. A lamellar corneal graft was performed using a 5.5 mm. disc of bovine cornea. This was fixed by direct sutures.

The post-operative course was uneventful. After 1½ months the temporal two-thirds of the graft was completely transparent. The nasal one-third showed some opacification. Three months later the condition was unchanged.

Case 2. A male aged about 70 showed bilateral corneal opacities and cataracts. The corneal opacity in the right eye was dense and central in position. A 5.5 mm. bovine lamellar corneal graft was placed in the right eye, using overlay sutures. Healing took place without trouble.

This graft became opalescent rather than transparent, but constituted a considerable improvement on the pre-existing condition.

DISCUSSION

The history of corneal heterografts is made up of a long succession of failures from the time of Wutzer who, in 1835, transplanted a sheep's cornea into one of his patients.[5] Payrau appears to have succeeded in breaking through the antigen–antibody barrier by his methods of preparing corneas for storage. This may have some application in other branches of surgery.

SUMMARY

Two cases are reported in which bovine corneas were successfully grafted into human eyes.

I wish to thank Professor Payrau of the Val-de-Grace Hospital, Paris for his help and encouragement and the Superintendent of the Far East Rand Hospital for permission to submit this article for publication.

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THE PROBLEM OF ABNORMAL RADIOLOGICAL LUNG PATTERNS

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In our work with the Pulmonary Function Unit we find that we have to contend with a constantly recurring problem, viz. the altered lung pattern on chest radiographs.

Descriptions used in the radiological literature have different meanings to different radiologists. Simon[1] states:

'That the writer of an X-ray report does not always say what he means is often due to confusion over the precise meaning of the terms which he uses.'

It has become evident to us that such vague terms as 'increased striate markings,' 'abnormal lung pattern,' 'increased reticulation,' 'honeycombing,' 'pulmonary fibrosis,' etc. should be more clearly defined or discarded and replaced by more adequate descriptions.

This paper tries to bring some order into a somewhat nebulous field and to explain the causes of some of the changes noted. It is by no means complete or exhaustive. We have not, e.g. tried to explain the reasons for the appearance of some lung shadows or to enumerate the disease processes which may produce identical appearances.

We have devised a descriptive scheme which is not cumbersome or laborious and which is sufficiently detailed to permit classification of any chest X-ray. Our experience has convinced us that diagnostic aid can be obtained from such a scheme, if it is used in conjunction with the patient's history, clinical and laboratory investigations and pulmonary function assessment. The correlation of a particular type of lung picture disturbance with a pattern of altered pulmonary physiology has increased our diagnostic accuracy; but many years of careful consideration and cooperation between the radiologist, the pulmonary physiologist and the pathologist with his whole-lung sections will be necessary to obtain perfection.

Occasionally a lung biopsy must be done, but all too often even the pathological findings are insufficiently typical for a firm aetiological diagnosis. This is not surprising as many different disease processes may give rise to rather similar end results, e.g. diffuse fibrosis.[2]

Before describing our classification, we must consider the structures and their shadows which combine to give the normal radiological lung pattern (Fig. 1A), and the reasons for alterations which occur in pathological conditions.

NORMAL LUNG MARKINGS

The normal branching linear markings of the lung are due to the pulmonary arteries and veins which subdivide and become progressively smaller between the hilar regions and the lung periphery. Together with their blood content they produce shadows of greater density than does the surrounding air-containing lung.

The bronchi and bronchioles, together with the pulmonary lymphatic channels, are not individually visible, but their presence adds to the background which forms the lung pattern, as does the peribronchial connective tissue framework of the lung, and the loose endothelial tissue which is interposed between the alveoli in the lung parenchyma.

The investing pleural sheaths of the lungs, the bony and the muscular thoracic cage, the subcutaneous tissue, the skin and the breasts add their share to the overall pattern seen on the chest X-ray.

Alterations and distortion of these structures by disease cause abnormal lung patterns requiring interpretation.

The translucency of the lung depends upon the amount of air and blood present. On deep inspiration the capacity of the pulmonary vascular bed enlarges, and the quantity of blood in the normal lung increases by about 50%, but the amount of air increases 2- to 3-fold. The result is a great increase in the transradiancy of the chest. The change in X-ray appearance between deep inspiration and deep expiration is, of course, most marked in the areas where the lung volumes are greatest, normally at the lung bases. In forced expiration the appearance may simulate very dense basal consolidation. A knowledge of the phase of inspiration prevents confusion. Changes in the relative quantities of air and blood either locally or throughout the lungs in disease will cause alteration of the normal lung appearances.

It is extremely difficult to define what constitutes early abnormality on pulmonary radio-

graphs. Sir John Parkinson[3] has stated, very aptly for the present discussion:

'We can only acquire good judgment of any departure from the normal by constantly looking at normal subjects for comparison, and even practice does not make perfect, for there are borderline cases where no arbitrary standards can apply.'

THE ARTERIAL COMPONENTS OF THE LUNG PATTERN

The branches of the pulmonary arteries radiating into the lung fields from the hila can normally be traced to within half an inch of the chest wall. The arterial branches closely follow the subdivisions of the bronchial tree, and each artery is usually in the same sheath as the corresponding bronchus. The bronchial arteries from the thoracic aorta give rise to a separate arterial system which follows the subdivisions of the bronchi in the same way as does the pulmonary circulation, but the two arterial systems cannot normally be differentiated radiologically.

Alterations in the arterial component of the lung field markings result from differences in pulmonary arterial blood flow and changes in pulmonary arterial pressure. These may be primarily of respiratory or circulatory origin. Extra-thoracic causes, e.g. arteriovenous fistulae, also play their part.

The pulmonary arterial component is increased by an increase of blood flow through the vessels of the lung. The arterial pattern is decreased by a diminution of flow, such as results from a decrease in the vascular bed of the lung. These alterations may involve both lungs entirely, or be localized to areas or segments. The situation sometimes arises where one lung or a portion of lung may be plethoric as the result of diversion of blood from the opposite diseased lung, or from diseased areas of the same lung.

Increased pulmonary blood flow will give rise to an accentuation of the pulmonary arterial lung shadows. This is particularly well seen in the congenital left-to-right vascular shunts, e.g. patent ductus arteriosus, atrial or ventricular septal defects, and large anomalous pulmonary veins draining into the right auricle or the venae cavae. These may result in hyperkinetic pulmonary hypertension. Although greatly increased pulmonary arterial blood flow may result from vigorous exercise, liver failure, Paget's disease, pregnancy, anoxia, pyrexia or anaemia, our experience has not shown any detectable changes in the lung field vascularity. This may be due to the fact that the normal pulmonary circulation will accommodate flows of up to 15 litres per minute without a rise in pulmonary arterial tension. In the hyperkinetic pulmonary hypertension mentioned, the arterial blood flow usually exceeds 15 litres per minute, resulting in some dilatation of the main pulmonary arteries and their large branches, the peripheral arteries remaining more or less normal or slightly more prominent. The pulmonary artery pressure in these conditions rarely exceeds a mean of 40 mm. Hg. In contradistinction to the 'hyperkinetic' or 'flow' hypertension, an obstructive pulmonary hypertension may be present with the vascular shunts mentioned. Wood[4] believes that the pattern of high pulmonary resistance in many cases is congenital in origin and is due to persistence of the thick-walled foetal type of arteriole. The 'obstructive' rise in pulmonary tension, however, may be due to secondary changes in the arterioles, e.g. intimal proliferation and/or medial hypertrophy resulting from torrential blood flow and increased pressures. Whatever the cause of the diminution in the pulmonary arteriolar bed, the blood flow drops rapidly and a marked rise in pulmonary arterial tension, exceeding a mean of 40 mm. Hg, results. With this rise in pulmonary arterial pressures the shunt may become balanced or reversed.

In this obstructive hypertension a different arterial pattern develops in the lung fields. The main pulmonary arteries and their larger branches are all markedly dilated with uniform attenuation of the peripheral vessels, giving rise to a peripheral translucency and paucity of vessels. This same picture may be seen in lung diseases associated with increased pulmonary arteriolar resistance. Bronchial and bronchiolar narrowing and occlusion may result from such diseases as tuberculosis, bronchiectasis, silicosis, emphysema and asthma, with resultant ventilatory embarrassment. According to Cournand,[5] hypoventilation and hypoxia not only increase cardiac output but also produce pulmonary arteriolar constriction. This diminution of the vascular bed may also result from diffuse interstitial fibrosis from any cause, and from obliteration of the vessels which may occur in bilharzia, lupus erythematosus, multiple vascular or neoplastic emboli, and polyarteritis nodosa. As already mentioned, the main pulmonary arteries and their larger branches are dilated with uniform attenuation of the peripheral vessels. This latter change, however, may be difficult to see on a plain X-ray film, being largely obscured by the causative pathological process, but tomography has proved of aid.

The pulmonary arterial changes described are primary, but arterial changes may be secondary to prolonged pulmonary venous or 'post-capillary' hypertension.

THE VENOUS COMPONENT OF THE LUNG FIELDS

The peripheral veins of the lung are in the septa which separate the lobules, while the arteries ramify in the lobules themselves. At about the level of the fourth bronchial bifurcation the veins and arteries become more closely related, only to become separated again near the hila, as they deviate to enter the left auricle.

The veins are not clearly distinguishable from the arteries in the straight chest radiograph, except for those draining the right lower lobe. These cross the shadows of the lower lobe arteries almost horizontally near the cardiac silhouette.

The upper lobe veins tend to lie lateral to the corresponding arteries, and run downwards and inwards towards a point over the dorsal spine 2–3 inches below the level of the hila. This direction is such that the main upper lobe veins cross the pulmonary artery trunks at right angles, a direction inconsistent with entry into these vascular channels. Further differentiating aids are that the venous tributaries join in a Y-fork at the level of the aortic arch,[6] and an almost horizontal tributary joins each main vein on its lateral side about one inch below this. The left upper lobe veins are usually better seen than the right, but are seldom as clearly seen as the arteries, being less well defined.

Any condition which obstructs the left auricle inflow or outflow of blood may result in an increase of pulmonary venous pressures, e.g. congenital anomalies or thrombosis of pulmonary veins, left auricular failure from mitral stenosis, left auricular myxoma, constrictive pericarditis, cor triatrium or auricular infarction, or left ventricular failure from any cause including systemic hypertension, myocardial infarction, aortic valvular disease and aortic coarctation.

In the erect position the lower lobe veins have a higher hydrostatic pressure than the upper lobe veins, and prolonged high pressure causes a reflex vasoconstriction of the lower lobe veins (and later the lower lobe arteries), diversion of blood to the upper lobes, with engorgement and prominence of upper lobe veins.[6] Above a left atrial pressure of 25 mm. Hg the upper lobe flow engorgement becomes less and less marked, particularly as arterial hypertension develops. This pulmonary artery pressure increase is often disproportionate to the venous pressure increase.

The characteristic lung vascular picture which results from post-capillary venous hypertension is particularly well seen in cases of tight mitral stenosis, where the lower lobe veins are small or invisible, and the upper lobe veins markedly engorged. The lower lobe arterial tree shares in the reflex vasoconstriction to give an avascular appearance of the lower lobes. With arterial pulmonary hypertension the main pulmonary vessels stand out in striking contrast to the peripheral attenuation and the prominence of the main pulmonary artery stem and the large left auricle complete the picture. With left auricular mean pressures above 18–25 mm. Hg, dilated interlobular septal lymphatics (Kerley 'B' lines) may be seen and in the 25–35 mm. Hg range alveolar pulmonary oedema may be visible when the fluid transudate is greater than can be rapidly drained away by the lymphatics.

THE LYMPHATICS OF THE LUNG

There are superficial and deep groups. The two sets of lymphatic channels are for the most part separate, communicating with each other at the pleural surfaces of the lung and in the hilar regions. The superficial lymphatics are situated in the pleura, whereas the deep lymphatics follow the pulmonary arterial branches, forming a network between the secondary lobules and the connective tissue septa.

When visible, the deep lymphatics ramify from the hila in a stellate fashion. These Kerley 'A' lines are from 2–5 inches long, threadlike, curved or angled, and must be due to the tangential projection of a deep thin plane of radio-opaque tissue bordered by aerated lung,[7] as any channel of circular cross-section of this size would be invisible on the chest radiograph. More frequently seen are the superficial Kerley 'B' lines, about one inch long, running inwards perpendicularly to the pleural surfaces, and due to fluid accumulation in the lymphatic tissue of the interlobar septa. These are best seen in the costophrenic angles where the lung is relatively free of confusing vascular shadows and where the venous pressure is greater because of the erect posture.

Oedema of the interlobular septal spaces may be the result of obstruction or engorgement of the lymphatics (as occurs in silicosis, neoplastic infiltrative spread, the lymphoid reticuloses and sarcoidosis) or may occur with

fluid transudation from lung capillaries with increased permeability (e.g. in head injuries, allergic lung involvement or exposure to irritant gases).

When the pulmonary venous pressure rises above the plasma osmotic pressure of about 25 mm. Hg, fluid transudation will occur into the connective tissue spaces of the lung, the draining lymphatic channels in the interlobar septa becoming visible as 'B' lines. When the transudate exceeds the drainage capacity of the lymphatics, alveolar oedema results, which is inevitable as venous pressures approach the mean 35 mm. Hg level.

The septal lines are most frequently seen in those conditions which cause a rise in post-capillary pressure, particularly mitral stenosis, but are also seen in left atrial tumours and less frequently in chronic and acute left ventricular failure. Kerley 'A' lines may precede clinical signs of left heart failure by 1–2 days until acute alveolar pulmonary oedema supervenes.

Correlation of upper lobe venous dilatation with the presence or absence of septal lymphatic lines and the degree of basal pulmonary arterial attenuation gives a moderately accurate assessment of the pulmonary venous (and arterial) pressures. The 'B' lines are related only to the venous pressures and do not reflect the pressures in the pulmonary artery. They may persist when venous hypertension is relieved, due to deposition of haemosiderin in the interlobular septa. They never arise as a direct result of primary pulmonary arterial hypertension.

THE BRONCHI, THE BRONCHIOLES AND THE AIR SPACES

The bronchi and the bronchioles are not visible in the lung fields as separate entities, but their presence contributes to the overall lung pattern.

Peribronchial tissue prominence from inflammatory oedema and cellular infiltration causes an alteration of lung pattern more commonly involving the lung bases. Gross thickening of bronchial walls in bronchiectasis may cause 'tramline' or tubular shadows, or the 'gloved-finger' shadows of Simon,[1] when their pus-filled outlines are thrown into contrast with the surrounding air-containing lung.

Bronchiolar involvement causes small areas of atelectasis seen as tiny rounded shadows, with dilated bronchiolar air spaces interspersed with these, the sharp outlines being the result of compression of normal lung tissue on the periphery. We believe that centrilobular emphysema can cause a similar lung pattern.

Interstitial pulmonary infiltrates and fibrosis produce variable patterns depending upon the behaviour of the pulmonary air spaces.

Multiple emphysematous blebs and bullae produce sharp linear patterns, often of a 'cystic' or large honeycomb type, as do multiple air-containing cysts and cystic bronchiectatic cavities.

We have been reluctant to apply the term 'pulmonary fibrosis' to widespread pulmonary pattern disturbances unless there is confirmatory evidence of cicatricial distortion of the vasculature or the pleura, or serial radiograph proof that the lung changes have been unaltered over a long period of time. It has been our experience that the loosely termed 'fibrotic' picture is reversible in many cases, as this may occur with interstitial pulmonary oedema, systemic lupus erythematosus and resolving lobar pneumonic consolidation.

THE PLEURA AND THE CHEST WALL

Changes in the pleura are superimposed on the underlying lung shadows and though confirmatory pleural thickening may lead one to suspect that a 'lung shadow' is due to overlying pleura, oblique fissure thickening and effusion particularly mimic changes in the lung in the postero-anterior projection. Genuine lung changes can be masked, as may happen in asbestosis, where tomography is sometimes required to demonstrate that pulmonary pathological changes lie beneath the greatly thickened basal pleura.

The skin and the subcutaneous tissues modify the X-ray appearances by altering radiographic penetration; or abnormalities may be projected upon the lung fields as apparently intrathoracic diviations from a normal picture. Awareness of this possibility can avoid unnecessary diagnostic embarrassment.

Breast shadows likewise cause apparent alterations in lung pattern which are easily recognized when the lower edges of the breasts are visible on the radiographs; but there may be some confusion in patients with small breasts, asymmetrical breasts or breasts well compressed against the film cassette, and particularly with heavy male breasts. Irregularities of breast structure projected on to the lung image may also mimic intrathoracic shadows. Oblique views and tomographs may be required on occasion.

We have found heavy pectoral muscle shadows in males to be a very frequent cause

of mid-zone 'veiling'. The lung fields of a heavily built rugby player must be considered in full awareness of the veiling propensities of his powerful chest musculature.

RADIOGRAPHIC TECHNIQUES

THE FILMS

The following views are obtained on patients referred for pulmonary assessment:

1. Postero-anterior radiograph in maximum inspiration.
2. Postero-anterior radiograph in forced expiration. This film requires an average increase of 5 K.V. over the inspiratory film.
3. Lateral radiograph in maximum inspiration.
4. Lateral radiograph exposed at the end of forced expiration.

An assessment of these films enables a fairly accurate estimate to be made of the total lung capacity, the vital capacity and the residual volume. Moderately gross deviations from the normal ratios can be gauged. Sufficient time must be allowed for the patient to inspire and expire for these radiographs, as even a minor degree of bronchospasm or airway obstruction may prolong the respiratory phases sufficiently to invalidate the information obtained from impatiently exposed radiographs.

5. Where pulmonary hyperinflation is suspected, or where the pulmonary vasculature is obscured by a pathological process, we usually do 2 tomographic cuts in the antero-posterior supine position, exposed with normal quiet inspiration, one cut at mid-distance, and one cut 2 cm. behind the mid-antero-posterior diameter. These are penetrated to show the lung field details rather than the less transradiant hilar structures. This is the method suggested by Fraser and Bates[8] to differentiate the hyperinflation of asthma from the organic vascular bed obliteration obtaining with emphysema.

6. Axial transverse tomograms are done of patients with marked kyphoscoliosis at the levels of maximum and minimum deformity. These cross-sectional views enable one to judge the volumes of the lung in each hemithorax more correctly than do the often confusing postero-anterior and lateral views.

THE QUALITY OF THE RADIOGRAPH

The quality of radiograph materially affects the appearances of the lung fields. The greater the penetration (kilovoltage), the less obvious are the lung markings and, conversely, the normal lung markings can be so altered by underpenetration as to appear abnormal to the unwary observer.

The ideal radiograph should be of such penetration that the upper 4 dorsal intervertebral disc spaces are visible, with 2 or 3 vertebrae faintly seen below the level of the upper limit of the aortic arch under favourable illumination.

In our experience, nodular and fine mottled shadows are poorly seen on 100 mm. miniature radiographs, while linear alterations in lung pattern are fairly obvious. Poorly defined, hazy, large shadows are often better seen on the miniature photofluorographs than on our full-sized films, which possibly accounts for the success of the reducing lenses used by some radiologists to examine large chest radiographs.

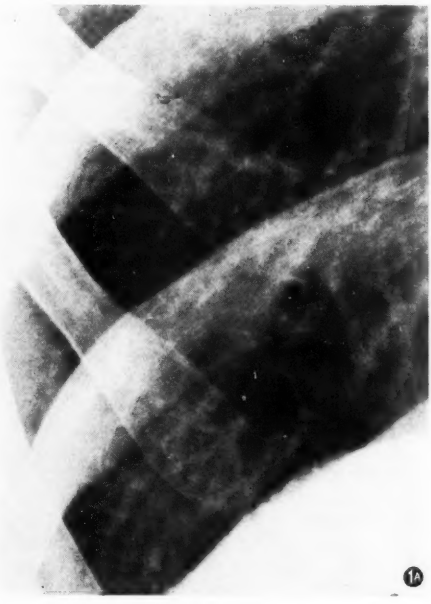


Fig. 1*A.* Normal lung pattern.

CLASSIFICATION OF LUNG PATTERN APPEARANCES

1. ALTERATIONS OF THE NORMAL LUNG PATTERN

(*a*) *Increased Prominence.* This is seen in any locally underinflated area, as well as in asthmatic attacks, inflammatory episodes, etc. One should beware of partly expiratory lung films with basal deflation simulating pathological changes.

(*b*) *Decreased Prominence.* This is seen in emphysema, hyperinflation of the lungs due to any cause, and diminished pulmonary vasculature in pulmonic stenosis. Hyperinflation is usually associated with an increase of peripheral translucency of the lung fields,

and very small peripheral vascular lines may be seen, mainly horizontal and in the lower lung zones, contrasted with the air-filled peripheral lung spaces. These vessels, usually invisible, can also be seen in very thin subjects.[6]

Use of 'vital capacity' films has demonstrated that decreased prominence of lung markings is frequently a normal phenomenon with voluntary, very deep inspiration, when other suggestive signs of emphysema (such as flattened diaphragmatic domes, prominent diaphragmatic digitations and increased retrosternal translucency) also become apparent. The expiratory films will show disappearance of these signs and the errors that may arise in assessment, and tomographs will demonstrate a normal, evenly tapering, pulmonary vascular pattern.

2. ADVENTITIOUS PULMONARY PATTERNING

This may be superimposed on a normal or increased background of lung markings, or may replace the normal lung pattern in varying degrees.

A. *Circular Shadows.* These may not be truly circular, but oval or vaguely rounded. These are subdivided arbitrarily according to the predominant size of shadow. The circular shadows may all be of comparable dimensions or widely different sizes may be present concurrently.

i. *Granular or Punctate.* This refers to multitudinous, pinpoint spots which would not be individually visible but combine by superimposition and proximity to give a ground glass or wash-leather appearance (Fig. 1B, 2. Bilharzia of the lung is a good example of this). We have seen a similar appearance in a case of systemic lupus erythematosus as well as in the early stages of the Hamman-Rich syndrome (Fig. 3).

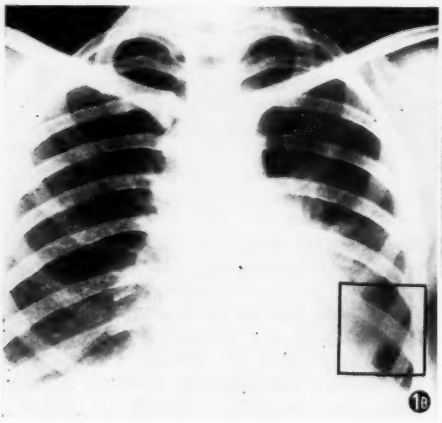
ii. *Miliary* (*Figs.* 4, 5). We have adopted Felson's criterion[9] for the use of this term i.e. an appearance similar to that of miliary tuberculosis rather than indicating the millet-seed size of individual nodules. The individual shadows are not seen until they are at least 2-3 mm. in size, but summation of smaller shadows of 0.5-2 mm. causes visible mottling. We regard 4 mm. as the upper limit of size denoted by the term 'miliary.'

Eighty-three causes of miliary mottling were listed by Scadding,[10] and 2 more were added by Blair[11] in 1954; but consideration of the X-ray appearances and distribution, the presence or absence of hilar lymphadenopathy or cardiac abnormality, together with a full knowledge of the clinical details, laboratory investigations and information about the chronicity or acuteness of the illness, depletes the differential diagnosis to useful and manageable proportions. We have found that a single diagnosis can rarely be given on X-ray features alone.

Scalene node or lung biopsy may be necessary for a definite diagnosis.

Twining and Kerley[12] list the relative frequency in Great Britain as:

1. Silicosis.
2. Miliary tuberculosis.



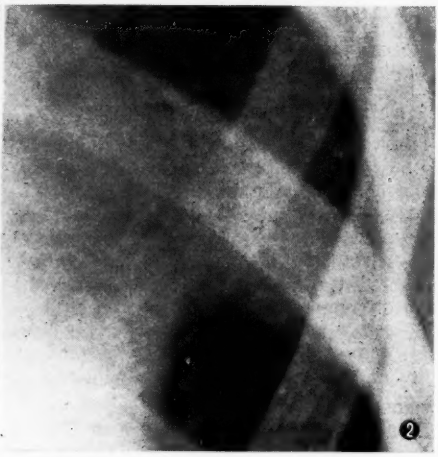


Fig. 1*B*. Granular shadowing at the left base giving rise to a 'ground-glass' appearance. A case of pulmonary parenchymal schistosomiasis.

Fig. 2. Contact print of the area enclosed by the square in *Fig.* 1*B*.

3. Rheumatic heart disease.
4. Sarcoidosis.
5. Malignant disease.
6. Miliary pneumonias and polyarteritis nodosa.
7. Primary haemosiderosis, mycosis, berylliosis and myloidosis.

Felson[9] lists 16 commonly occurring acute onditions which give rise to miliary shadows.

iii. *Nodular* (*Fig.* 6). This term is used or opacities of larger than miliary size and which may be well defined (as in blood-spread econdary neoplastic deposits) or poorly outined (as in some cases of polyarteritis nodosa nd the evanescent shadows of pulmonary eosinophilia or the pulmonary migration stage of ascariasis, which is not uncommonly seen in South Africa).

B. *Linear Shadows.* These include:

i. *'Hairlines'.* This description includes the thinner Kerley 'B' lines of visible interlobar septa (Fig. 7A), the walls of bullae, as well as the sharply defined lines seen in some forms of pulmonary fibrosis and 'honeycomb' lung.

ii. *'Crayon Lines'* (*Fig.* 7B i). This description denotes well-defined, thicker lines which we have seen in cases of aspiration

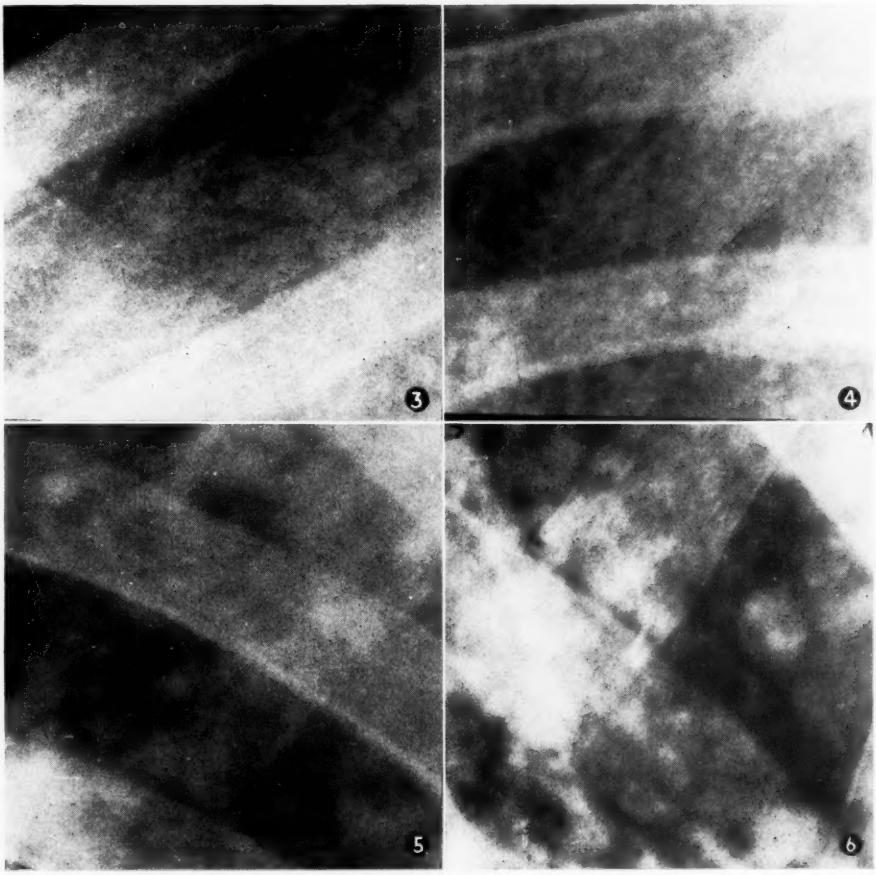


Fig. 3. Right basal granular shadowing. Contact print of a case of early idiopathic pulmonary interstitial fibrosis.

Fig. 4. Fine miliary mottling. Acute miliary pulmonary tuberculosis. Contact print.

Fig. 5. Left midzone. Coarse miliary mottling. A case of pulmonary *Monilia albicans* infection.

Fig. 6. Small nodules. Contact print of left base of a case of blood-borne pulmonary metastases. Primary seminoma of the testis.

fibrosis and bronchiolitis, as well as bronchiectasis and post-inflammatory lung damage. These lines are clearly distinguishable from branching blood vessels.

Fig. 7A. Kerley 'B' lines in a case of gold miner's pneumoconiosis.

iii. *Poorly Defined Lines.* This connotation is used for want of a better term to describe the shadowing which one cannot entirely distinguish from lung peripheral vascular branching, but which is definitely abnormal and new, not being an exaggeration of normal markings. We are reluctant to place cases into this group without first excluding such causes as slight underpenetration of the chest radiograph or heavy soft tissue or pectoral shadowing.

Linear Patterns. New lines may be long or short. We sub-classify them further into those which interlace and cross to form a true network and those which remain discrete. Examples of the latter are the 'B' and 'A' lymphatic lines of left heart failure, lymphangitis carcinomatosa and some pneumoconioses. The network type of patterning may be fine as in anthracosis (Fig. 7c), the Hamman-Rich syndrome and early pulmonary scleroderma or cause a coarse honeycomb appearance as in histiocytic pulmonary reticulosis (Fig. 8), (xanthomatosis and pulmonary eosinophilic granuloma), cystic bronchiectasis and pulmonary cystic disease (Fig. 9).

C. *Combinations of Linear Shadows and Circular Shadows* (Figs. 10-12). Such combinations frequently occur, and the linear effect may be due to a superimposition phenomenon of myriads of circular fine shadows in the various layers of the lungs; or distinct linear shadows may co-exist with opaque dots. Follow-up radiography may reveal that an adventitious pulmonary mosaic pattern previously thought to fall into the group of poorly-defined lines is, in fact, due to miliary mottling.

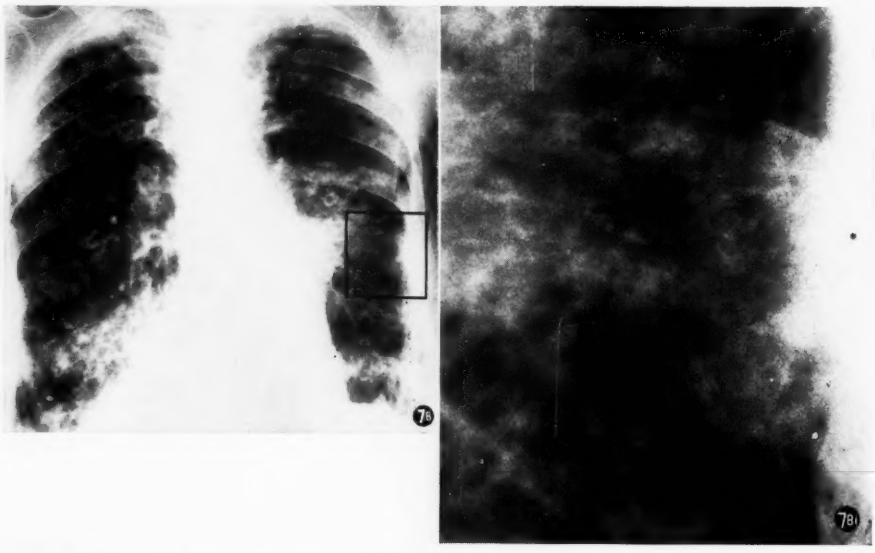
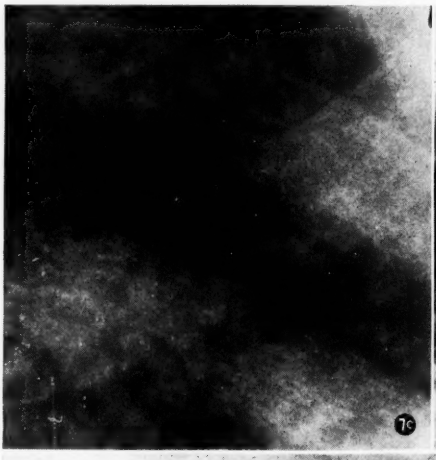
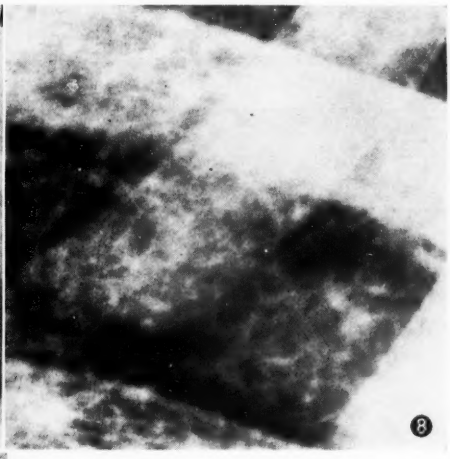


Fig. 7B. 'Crayon-line' shadowing in a case of saccular bronchiectasis which was widespread.
Fig. 7Bi. Contact print of the area enclosed by the square in the left midzone of *Fig. 7B.*

Simon's tabulation[1] of very small circular shadows into groups having 'reticular pattern absent or slight' and 'reticular or net-like pattern marked' well illustrates how the radiological pattern overlaps.

Pulmonary function tests, blood and serological investigations, sputum tests, scalene node biopsy, muscle biopsy and even lung biopsy may be necessary to establish a definite diagnosis.





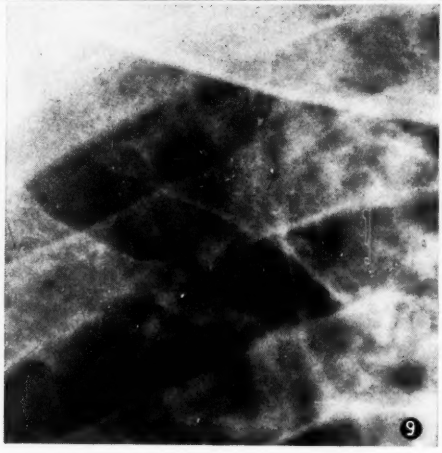


Fig. 7*C*. Left infraclavicular zone. 'Hairline' shadows giving a fine reticular appearance. Coal miner's pneumoconiosis. (Contact print).

Fig. 8. 'Hairline' shadowing of a honeycomb nature. A case of pulmonary eosinophilic granulomatosis. The patient also had diabetes insipidus.

Fig. 9. 'Hairline' shadows in the right upper zone of a case of congenital cystic disease.

CONCLUSIONS

In the vast majority of cases it has been our experience that it is impossible to give a definite diagnosis on the X-ray features of altered lung pattern alone.

A detailed, searching history is imperative.

Alterations in the cardiac contour may give a possible clue.

Careful attention to associated skin lesions, sudden changes in scar tissue, the presence of diabetes insipidus or associated cystic bone changes may be of assistance.

SUMMARY

1. The confusion in terminology to describe abnormal lung patterns is commented upon.

2. Normal lung markings are described.

3. The causes for alterations in the arterial and venous patterns are given.

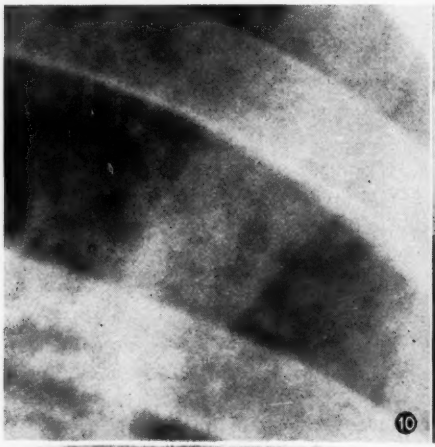
4. The reasons for the appearance of the lymphatic lines in the lung field are enumerated.

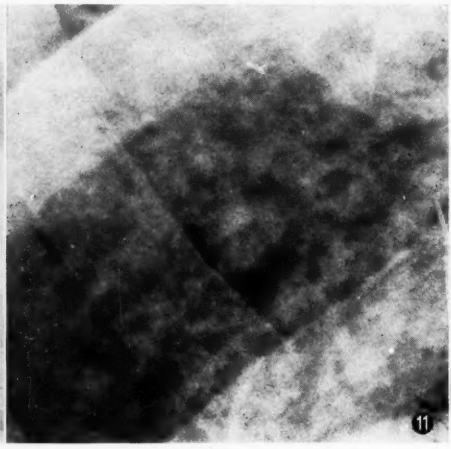
5. The effect of peri-bronchial and interstitial tissue accentuation on the lung pattern is noted.

6. The radiographic techniques employed in the Pulmonary Unit are described.

7. A classification for alterations in the normal lung pattern and of adventitious pulmonary patterning is suggested.

8. The need for special investigations and consultation between the radiologist and the clinician is emphasized.





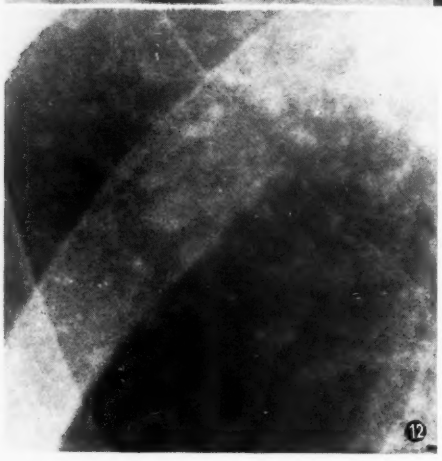


Fig. 10. Poorly defined linear reticular pattern with some miliary mottling. The left mid-zone of a case of sarcoidosis.

Fig. 11. Combination of poorly defined and 'hairline' patterning in a patient with scleroderma. This patient also had a lower oesophageal stricture and a stenotic lesion of the third part of the duodenum.

Fig. 12. Combination of punctate and 'hair-line' shadowing at the right lung base of a carpenter with imbuia-wood dust allergy.

We are deeply indebted to the physician and pathologist members of the Pulmonary Unit team for their suggestions and constructive criticism.

Our thanks are due to Miss M. W. Tompkins for the radiographic reproductions.

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HYPOTENSION AND SHOCK

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Samson Wright (9th ed.) states at p. 237:

1. The mean aortic blood pressure is one of the main factors which control the coronary circulation. Thus, in a denervated heart lung preparation (dog) an increase in mean blood pressure from 50 to 130 mm. Hg may increase the coronary flow from 20 to 250 c.c. per minute. A low blood pressure from any cause similarly leads to an impaired blood supply through the coronaries, and defective nutrition of the heart, which further depresses the state of the circulation.

2. At p. 306: Cerebral blood flow is diminished by a fall of arterial blood pressure reflexly produced by carotid sinus stimulation. The blood flow through the brain varies directly with the level of arterial pressure.

At p. 314: A pressure which is much below normal is unable to drive an adequate amount of blood to the brain against the force of gravity.

3. The blood flow through the kidneys (as through other organs) depends on the cardiac output, the general arterial blood pressure, and the calibre of the local arterioles and capillaries.

These ' unarguables ' are drummed into one's head during one's training in physiology. They are stressed again and again during the clinical years, so that by the time the intern year has passed, this concern with blood pressure and its maintenance at a normal level has become almost an obsession.

We propose in this paper, in the light of experience gained by the administration in a large number of hypotensive anaesthetics, to criticize these beliefs, and perhaps to present them in a different perspective, so that blood pressure will not be viewed as an entity in itself, but in relation to the physiology of the entire organism.

Our series commenced in July 1951, and up to May 1959 we (H. B. in collaboration with L. M.) had completed over 3,000 cases of hypotensive anaesthesisa. The age limits of the patients were between 12 and 86 years. The large majority were plastic and maxillo-facial cases, with some ear-nose-throat and neurosurgical cases. We relied on our own clinical judgment whether the patients were fit for hypotensive techniques.

However, despite the fact that the number of cases above the age of 50 contributed 30% of the series, and that a significant number of them were arteriosclerotic and hypertensive, no pre-operative ECG's or any other clinical investigations were done, only those with known coronary disease being ruled out. *All* the cases in this series were allowed to breathe spontaneously, anaesthesia in the large majority being maintained by 100% oxygen and ether.

The drugs used to produce the hypotension were primarily hexamethonium and later Arfonad and Ansolysen. Often a combination of all these drugs was used and sometimes, when hypotension was still inadequate, we administered up to 10 c.c. of Procaine Hydrochloride 2% or Pronestyl intravenously.

The average duration of hypotension was one hour, and although we have maintained hypotension for 2½–3 hours, we tried to set a limit of 1½ hours for the very low pressures, because recovery (especially using an agent as potent as ether) was slow. However, even in long procedures the main body of the operation could be completed in the scheduled time, and we allowed the pressure to rise slowly thereafter. With increasing experience, we were able to produce a return to consciousness within 15 minutes of the end of surgery.

We tried in all cases to keep the circulating blood volume within normal limits. Losses of between 100–150 c.c. were well tolerated by the patient. In lengthy major procedures, e.g. forehead rhinoplasties, maxillary tumours with resections, etc., we ran a slow blood drip, but this was more for our benefit than for that of the patient. The drip was discontinued when the patient left the theatre, the average amount used being in the region of 200 c.c.

In other procedures when there was bleeding despite adequate hypotension, we ran a slow drip of 5% glucose in water for the duration of the operation.

We set no limit to the number of hypotensive anaesthetics for any one case. Several of the patients had more than 2, while one patient aged 20 had 8 of these anaesthetics in the course of a year, and another in the same age group 9 over a period of 18 months.

In the initial series, using hexamethonium, we encountered tachycardia in almost all the young, fit, normotensive patients, but we can-

not agree with Johnston (*Anaesthesiology*, September 1958) that the tachycardia did not allow normal ventricular filling during diastole; we found cardiac output adequate.

Strangely enough, in the elderly hypertensive patients tachycardia was rarely encountered using hexamethonium. The pulse rate in the great majority of these cases was normal or even slightly slower than normal. Since the advent of Arfonad and Ansolysen (used for the last 2,500 cases), tachycardia has not been a feature.

Post-operative shock, despite using an anaesthetic agent as potent as ether, was completely absent, the appearance of the patient corresponding to the 'hexamethonium man' of Paton, with a dry, warm and pink skin, and dilated veins. This disappearance of shock has been aptly described by Paton with his concept of 'a controlled circulation effected by sympathetic blockade at ganglionic level.'

It became apparent early on that the blood pressure itself could not be used as an indication of the well-being or otherwise of the patient. It proved helpful *only* when taken in conjunction with the following signs.[4]

1. *Breathing*: If the breathing is regular with no tracheal tug, all is well as a rule. If the breathing is irregular or a tracheal tug is present, cerebral anoxia may be responsible and the pressure should be raised.

2. *The Skin*: The skin should be pink, dry and warm with vasodilation present. If cold, mottled or bluish with vasoconstriction, the pressure should be raised.

3. *Operation Site*: With adequate anaesthesia, oxygenation and hypotension and a clear airway, the operative site should be comparatively dry with little capillary bleeding, and the colour of the blood should be pink.

Cyanosis in the wound is an indication to reverse the hypotension.

4. *Peripheral Circulation*: The lobes of the ears, the finger nails and the toe nails should be pink at all times, with normal emptying and filling of the capillaries on pressure.

In the initial series of 250 cases we first tilted the patient, and then gave the hexamethonium which, in this manner, produced a rapid, uncontrollable fall of blood pressure and which in approximately 70% of these cases was unrecordable either by auscultation or palpation. In order not to inconvenience the surgeon by tilting the patient backwards and forwards (aptly described as akin to operating on a tossing ship), we placed *complete* reliance on these other aforementioned signs with absolutely no ill-effect to the patients.

In this whole series there were *no* operative or post-operative coronary incidents, *no* cerebral thromboses, *no* kidney or liver dysfunctions, and *no post-operative morbidity or mortality*.

To consider in more detail the effects as we found them, of the hypotension on the vital organs:

The Brain. In all neurosurgical cases the cerebral circulation under direct vision was adequate, as ascertained by the blood flow, the colour of the blood and the colour in the wound, and by the results of operation.

When we consider that the blood pressure at a given point in the reverse Trendelenburg position, is 2 mm. Hg lower than that at heart level for every inch above this level, that most of these patients were in steep reverse Trendelenburg, that the blood pressure at heart level was often below the so-called minimum of 60 mm. Hg, and that there were no post-operative cerebral complications, it seems that induced hypotension, provided attention is paid to all signs, does not affect the brain.

As Forbes-Fog demonstrated, the brain may be 'pressure regulated.' With low, arterial pressures regardless of how achieved, cerebral vasodilation is the response. With high arterial pressure cerebral vasoconstriction is seen. The vessels of the brain are apparently designed to regulate the resistance to flow in their own circulatory area. We think that the actual blood flow in induced hypotension is relatively constant, or even better, as determined by the vasodilation.

Coronary Flow. No experimental work was done on the coronary flow in this series, but the operative and post-operative results inclined us to the views of Hackel, Sancetta and Klenerman and Eckenhoff *et al.* These workers, under experimental conditions, have reached the conclusion that under conditions of reduced peripheral resistance, the reduction in cardiac work is relatively greater than the reduction in coronary flow. When the work load on the heart was reduced by half, it was found that the coronary flow was reduced by only one third. In other words, the coronary flow in ganglionically produced hypotension is relatively greater than in the normotensive state.

We agree with Rollason and Hough[3] that, in ECG studies during hypotensive anaesthesia, the action of the heart is not seriously affected in the pressure range investigated, and that the reduction in coronary flow is *more* than

compensated for by a reduction in cardiac work.

One case of interest which they show, with malignant hypertension and a classical left ventricular strain, reverted to a virtually normal tracing during the low-pressure phase. Schwartz *et al.*[6] suggests that the critical level of coronary flow is as low as 10–15 mm. Hg.

Respiratory System. The air passages are dry and relaxed with dilatation of the bronchioles in all patients including those with bronchiolar constriction. It was significant how smoothly the heavy smokers tolerated ether.

Kidneys. With conventional anaesthesia kidney function may be temporarily suppressed, as gauged by secretion of urine with resumption of urine formation at the end of anaesthesia. Fifty cases under hypotensive anaesthesia were compared with 50 cases under ordinary anaesthesia. All patients were catheterized just before commencement of anaesthesia and the catheters left in. Forty-two cases under hypotensive anaesthesia secreted fair amounts of urine during operation despite, in some cases, extremely low heads of pressure compared with 23 cases in the control series. While this is not conclusive evidence, we think that kidney function is not only *not* interfered with by ganglionic blocking agents, but may even be improved.

Liver Function. No liver function tests were done, but a follow-up over the years has not revealed any case of liver damage.

At this point it must be stressed again that all these cases were breathing spontaneously. The physiology which obtains when hyperventilation and positive pressure are added to the ganglion-blocking agent to produce hypotension, is another matter entirely.

From all our observations, on practical grounds we believe that provided oxygenation is maintained, even at extremely low heads of pressure produced by the ganglion-blocking agents, vital functions of the brain, liver and kidneys are not interfered with, and the coronary flow is increased in relation to the cardiac output.

In other words, in ganglionic blockade, despite an extremely low blood pressure, the well-being of the patient is not only maintained, but he is being protected against shock.

We stress again:

(*a*) The coronary flow, despite the low aortic mean pressure, is relatively greater than in the normotensive state;

(*b*) The cerebral flow is *not* diminished by the fall in blood pressure;

(*c*) There is *no* interference with liver or kidney function.

I should have realized all this in 1941 when I did a series of 78 cases under epidural block. These included 25 bad risk cases, e.g. acute abdomens in elderly patients, intestinal obstructions, and other cases with shock. Although the blood pressure of some of these patients was already low pre-operatively, and was further lowered by the epidural block, sometimes to alarming levels, and although our restoration therapy could not compare with what it is to-day, these patients did extremely well. In *no* case was a vasopressor used, and there were no adverse results attributable to the anaesthetic. In fact, the surgeons were so pleased with the epidural anaesthesia that if the time factor and the occasional failure had not limited its use, it would have become the anaesthetic of choice in most bad risk cases.

Gardner[2] agrees with this. He says:

'We are not unduly concerned when the systolic pressure falls even well below 60 mm. Hg, provided that the colour remains good, the carotid pulse is satisfactory, and the pupils are small. Oxygen was not as a rule administered. During the early part of our experience with epidural analgesia it was our aim to lower the blood pressure to between 60 and 80 mm. Hg systolic. Latterly we have not worried even when it has fallen well below 60 mm. Efforts to raise the blood pressure were very rarely made during or after operation under epidural analgesia. It has been clearly shown that the coronary blood flow is more closely related to the metabolic demands of the heart than to the arterial blood pressure, so that the lowered blood pressure in point of fact eases the strain on the coronary blood flow.'

If all this is still not regarded as producing sufficient evidence that ganglionic blockade produces favourable conditions even at very low pressures, we now have Fluothane. According to the volume of clinical data this may well be the anaesthetic of choice for surgery in elderly patients with advanced pulmonary and cardiovascular disease, a group which has been particularly refractory to most other agents and techniques (Johnstone).[7] The reason for this claim is that Fluothane, besides providing ideal operating conditions, *appears to prevent shock and circulatory collapse.* For the present it would be reasonable to assume that Fluothane suppresses sympathetic activity at some level, presumably ganglionic. In reasonable concentrations it produces a physiological state with peripheral vasodilation, a *lowered blood pressure and a diminished work load on the heart.*

To summarize, anaesthesia to which ganglionic-blocking agents are added, epidural

anaesthesia and anaesthesia with Fluothane, which all produce hypotension, not only protect against shock, but even when shock is present afford more protection against it than does conventional anaesthesia.

To this formidable array spinal anaesthesia can be added. We all know from experiments done by a host of workers that spinal anaesthesia provides much longer protection against shocking procedures than ordinary methods. From this we can conclude that 4 methods of anaesthesia which *all* produce hypotension, protect against shock. This seems paradoxical because in the past hypotension has always been looked upon as a precursor, or an integral part, of shock.

However, we must realize that blood pressure is *not* an index of capillary circulation. All the foregoing clinical observations and experimental evidence prove that tissue flow and arterial pressure cannot be directly correlated and, in fact, may be completely divorced from each other.

Shock and Blood Pressure. With these facts in mind let us attempt to assess the role of the blood pressure in shock.

In shock from any cause we know that vasoconstriction is a fundamental mechanism, and while we agree that a falling blood pressure is an indication of advancing shock, we do not think that this vasoconstriction is activated solely to maintain blood pressure.

The falling blood pressure in shock is only *one* of a series of physiological mechanisms taking place in the body due to changed conditions, and I maintain its restoration to normal by means of a vasopressor will *not* benefit the patient if the rest of the body physiology is not restored. It can, in fact, transform an impending case into a case of irreversible shock. The sudden restoration of blood pressure by a vasopressor does not assist other restorative measures which are being taken, e.g. blood or plasma transfusions. In fact, by increasing the peripheral constriction it provides a mechanical bar to adequate transfusion. Hereby a false picture is produced which lulls the anaesthetist and the surgeon into a feeling of security *because the blood pressure is normal.*

If the blood pressure falls according to a physiological principle, then there is no rational basis for asserting that it should be restored to a normal level with a vasopressor drug, thereby producing an unphysiological state.

A patient is given a spinal anaesthetic. A ganglionic blockade up to the level of the spinal anaesthesia is produced. The blood pressure falls—but only because the peripheral resistance is reduced in accordance with the ganglionic blockade. The work load on the heart is accordingly diminished.

Here we have a physiologically produced condition with all the component parts acting as they should. But what do we do? Someone stipulated years ago that the blood pressure falls in spinal anaesthesia and that the cerebral and coronary flow depends on the blood pressure, and blindly through the years we have accepted this without query or analysis. So we inject Methedrine, Wyamine, or Neosynephrine, and restore the blood pressure to its normal level, or even above this. The fact that we have transformed a physiological into an unphysiological state means nothing; the blood pressure is normal and all is well!

Now to consider shock and the vasopressors. It is accepted that the early physiologically produced factor in all forms of shock (whether it be due to trauma, haemorrhage, intestinal obstruction, coronary occlusion, anaphylaxis, surgery or anaesthesia) is peripheral vasoconstriction mediated through the CNS. Thus one could reasonably assume that vasoconstriction *per se* is a fundamental mechanism by which the body responds to whatever is causing the shock.

It seemed logical, then, that if the peripheral vasoconstriction, i.e. the body's physiological response, could be increased by means of a vasopressor, it would benefit the patient. This has been universally accepted, but is open to criticism. If the vasopressors only produced a peripheral constriction no one could argue with their beneficial role. Unfortunately, at the same time they produce a vasoconstriction in most of the vital organs of the body, which can only produce deleterious effects.

Let us first consider the effects of the vasopressors on the coronary flow. They increase the peripheral resistance and raise the blood pressure and thereby increase the work load on the heart. The aortic mean pressure is increased and so is the contractility of the heart muscle, thereby producing a physiological increase in coronary flow. However, workers in Philadelphia, experimenting with catheters tied into the coronary vessels, demonstrated that the vasopressors produced a *local constriction* of the coronary vessels which offset any increase in coronary flow produced physiologically. In fact, they showed conclusively that coronary flow in relation to the increased work load on the heart is inadequate. They estimated that both adrenaline and noradrena-

line introduced artificially into the body increased the work load on the heart by 90%, while the other less potent vasopressors such as neosynephrine, Methedrine or Wyamine increased it by 47%, while none of them increased the coronary flow.

We know that the liver, kidneys and intestines become pale and bloodless in shock. We also know from recent studies of tissue metabolism that anaerobic metabolism, produced by anoxia due to intense vasoconstriction, is the factor in producing irreversibility. These metabolites have recently been isolated from the bowel and the liver.

Now consider all the effects of the most widely used vasopressor, noradrenaline. It increases the force of the myocardial contraction, usually reduces the cardiac output, has no effect on the coronary flow, and produces a vasoconstriction of the brain, of the lungs (with concomitant pulmonary oedema), of the kidney, and of the liver and bowel (with increasing production of the metabolites mentioned above). *But—it raises the blood pressure*—and so it is widely used to combat shock.

I humbly submit that it often converts a case of impending into a case of irreversible shock, despite the great advance in supportive therapy. Foster, Collins and Scott,[8] working on renal blood flow in haemorrhagic shock, found that in spite of a normal blood pressure maintained by noradrenaline, 8 of 10 dogs developed irreversible shock.

As regards the other vasopressors, adrenaline produces variable effects on coronary tissue flow, but its constrictor effect on the kidneys and its effect of producing cardiac arrhythmias limits its use. If vasopressors have to be used, the best would seem to be Methedrine and Wyamine, which produce a raised blood pressure by cardiac stimulation, in spite of initiating vasodilation. No reduction of blood flow to any organ, including the kidneys, is liable to occur. However, even with these there still seems to be some disproportion between coronary flow and work load on the heart.

As we stated before, vasoconstriction (mediated through the sympathetic nervous system) is the early physiological response in all forms of shock. The factor common to *all* forms of shock is a reduction of cardiac output, whether this be primary, as in coronary occlusion, or secondary to a deficient venous return, as in haemorrhagic or traumatic shock.[1] Since this is the earliest factor common to all the entities, one may postulate that an acute reduction in cardiac output is always the basis of the shock syndrome. With this assumption we may define shock as 'the sympathetic response to an acute reduction of cardiac output, primary or secondary.'

What then is the toxic factor? Why, if after a time lapse, we transfuse an amount of blood equal to, or even greater than the amount lost, does irreversible shock take place? Why, even after correcting the cause of the shock syndrome, and aiding it with supportive therapy expertly administered, are our efforts often in vain? *The time factor seems to be of paramount importance.* Clark[9] in 1957 suggested that the failure of response to blood transfusion was due mainly to *'too little blood too late.'* Wiggers *et al.*[10] postulated that if the blood pressure, as a result of haemorrhage, was maintained at 60 mm. Hg for 90 minutes, followed by 35 mm. Hg for 45 minutes, irreversibility, as manifested by resistance to transfusion, occurred.

As we have tried to demonstrate, blocking of the sympathetic nervous system with its consequent prevention of vaso-constriction, produced adequate protection against shocking procedures. The ganglion-blocking agents, epidural and spinal anaesthesia, and Fluothane, which all produced a partial or complete sympathectomy with vasodilation, protected against shock.

Erlinger and Gasser[11] were able to produce irreversible shock by prolonged intravenous injection of adrenaline into animals which had not suffered blood or fluid loss. Scholz *et al.*[12] have also obtained consistent results in producing irreversible shock by the intravenous injection of adrenaline.

When we consider all this we are justified in concluding that the factor which causes the irreversibility in shock, in other words, the toxic factor, *is the prolonged vasoconstriction.* Our treatment must then be aimed at:

1. Restoring the cardiac output to normal levels by supportive therapy where a hypovolaemia exists.
2. Preventing the noxious effects of prolonged vasoconstriction:

(*a*) As in (1), where supportive therapy has for some reason been delayed;

(*b*) In cases where a normovolaemia co-exists with the vasoconstriction, e.g. in coronary occlusion and 'medical shock.'

The drug we have chosen to counteract the effects of the prolonged vasoconstriction is Arfonad. Our reasons are:

1. It is given in a 0.1% or less concentration by intravenous drip, and minute doses can be given this way. This is important in any method preaching a revolutionary therapy;
2. It does not cause tachyphylaxis or tachycardia;
3. In our earlier experiments in hypothermia we often found pulse irregularities on cooling in the

36–30°C. orbit. Whenever Arfonad was administered to these cases, the irregularity disappeared. ECG's taken of these cases demonstrated that Arfonad has a *direct beneficial effect on the heart muscle.*

The Arfonad solution (0.1%) was administered very, very slowly, ignoring the blood pressure, till the constriction peripherally was replaced by dilatation. It was then regulated to maintain this state, all the time keeping up with other supportive therapy. We knew, from our previous experience, that brain, liver, kidney and coronary blood flow would be improved, whatever the pressure.

It would be attractive at this point to be able to quote a large series of cases in support of our theory. Fortunately or unfortunately I can only present 8 successful cases. These were all surgical post-operative cases, viz. 3 gastrectomies, 2 colectomies, one hemicolectomy, one intestinal obstruction, and one exploration of the common bile duct. Fluid, blood and plasma therapy were used in all, together with the vasopressors and intravenous hydrocortisone with no response.

These cases were very gratifying in that they recovered when it seemed certain that they must go into irreversible shock. I have tried to convince my surgical colleagues that this method holds promise, but old habits die hard and opposition has been intense. However, a colleague with more amenities has reported another 10 successful cases, including one which was on Arfonad for 36 hours.[5] Another reports an interesting case of malignant hypertension who was admitted comatose with a large cerebral thrombosis. Despite a falling blood pressure with constriction and cyanosis of the periphery, and irregular breathing, it was decided to try Arfonad. His blood pressure fell even more, but his clinical condition improved immediately with warm, pink and dry extremities and regular breathing. This improvement was maintained for 10 hours on an Arfonad drip but, unfortunately, a relieving Registrar was not told of the experiment and on finding the blood pressure low, immediately substituted a Levophed drip for the Arfonad. The patient died within an hour.

I have asked for this method to be tried in coronary thrombosis with shock, but so far the only response by the physicians has been one of amused tolerance. In this condition we have an acute reduction in cardiac output which is primary. The central mechanism, the heart or pump, is damaged. Surely it is logical to try and rest this pump by decreasing its work load? If at the same time one can increase this pump's blood supply in relation to its work load, and also maintain or even increase the circulation in the other vital organs, all of which can be achieved by ganglionic blockade using Arfonad, can this method be completely ignored? How many times, in discussion with physicians, has one been told: 'It is kidney failure which kills in coronary occlusion,' and 'You must have a certain head of pressure to maintain the blood flow through the kidneys.'

The blood pressure is not an index of capillary circulation. Tissue flow and arterial pressure cannot be directly correlated. The use of noradrenaline in coronary occlusion with shock, with its increase of vasoconstriction, its concomitant increase of work load on a damaged heart (90%), without increasing the coronary flow is, in my opinion, and in view of the beneficial results claimed, only an indication of the amount of assault which even a severely damaged heart can stand.

I have tried to obtain experimental animals to either prove or disprove my theory, but so far have not been successful. I hope that someone who may read this and who has more laboratory facilities, will take up the challenge. It is only an idea but, as Professor Wangenstein of the University of Minnesota states,

'The most fundamental requisite of a research project is an idea.' I have set out my ideas—will someone develop them for me?

I am indebted to Dr. L. Melzer for his help and co-operation at all times with the hypotensive anaesthesia and to Roche Products (Pty.) Ltd. for supplying the Arfonad, and to Mr. J. F. Paterson of that firm for his encouragement and co-operation.

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NOTES AND NEWS : BERIGTE

Dr. Roy Morris has returned from overseas where he visited medical units in New York, Boston and London and has now resumed practice.

* * *

Dr. M. U. Milunsky has commenced practice as an anaesthetist at 305 Harley Chambers, Jeppe Street, Johannesburg. (*Telephones*: *Rooms*: 22-3886; *Residence*: 25-7793).

* * *

Dr. A. N. Sacks, of East London, has been made an Honorary Member of the British Society of Medical Hypnotists.

* * *

Dr. Isidor Kaplan, Physician, has moved his Consulting Rooms to 921 Rand Central, Jeppe Street, Johannesburg. The telephone number remains the same, i.e. 22-4546.

THE WELLCOME TRUST GRANT TO THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON

The Wellcome Trustees have made a grant of £50,000 sterling (approximately 140,000 dollars) to the Massachusetts General Hospital, Boston, for the establishment of a Henry S. Wellcome Research Chair in Medical Science. The Professor will be chosen by a special committee of the Massachusetts General Hospital, Harvard University and the Massachusetts Institute of Technology, from a number of workers who have already achieved a high scientific reputation for their researches. The appointment will be made for 10 years.

This grant was announced in Boston on 7 June, in relation to the preparations for the 150th Anniversary of the founding of the Massachusetts General Hospital which falls next year.

This is the largest single grant to be made by the Wellcome Trustees to a medical research centre in the United States. In 1956 they made a grant of nearly £25,000 (69,000 dollars) to the University of Pennsylvania to provide a Wellcome Associate Research Professorship of Anesthesiology for 5 years, and earlier in the present year they made a grant of £15,000 (42,000 dollars) to construct a laboratory for cardiovascular research within the Department of Medicine at Johns Hopkins Hospital, Baltimore.

PREPARATIONS AND APPLIANCES

CLORPACTIN WCS-90

Westdene Products (Pty.) Ltd. announce the introduction of *Clorpactin WCS-90*, manufactured by the Guardian Chemical Corporation of America.

Clorpactin WCS-90 (monoxychlorosene) is the nearest approach to the ideal antiseptic so far discovered. Both its liquid and vapour phases are lethal to every single known organism whether bacterium, fungus or virus. Even thermophilic spores are killed within one minute and destruction of any simple organism such as *Staph. aureus* takes place in a matter of seconds. *Clorpactin WCS-90* is also completely effective against *M. tuberculosis, Strep. pyogenes, B. pyocyaneus, B. anthracis, B. coli, Trichomonas vaginalis, Salmonella, Shigella, P. vulgaris, H. pertussis, Brucella, Proteus vulgaris*, etc., as well as yeast and fungi, etc. Yet there is complete absence of toxicity, irritation or sensitization. In addition, *Clorpactin* has pronounced deodorant, wetting and penetrating properties.

Clorpactin is a purified grade of an organic hypochlorous acid derivative, buffered and stabilized and supplied in the form of a white water-soluble powder. It is now available in boxes of 5 vials each containing 2 g. For use, the contents of one 2-g. vial are usually dissolved in 500 c.c. of lukewarm distilled or tap water (0.4% solution). Solutions are rapidly de-activated by exposure to organic solutions and discharges, so that adequate quantities must always be brought into frequent contact at the desired site of action. Copious amounts of *Clorpactin WCS-90* solution should therefore be flooded as frequently as possible over the entire area either with a syringe or by means of gravity flow.

Clorpactin has been found to be extremely effective for skin preparation prior to surgery; to reduce the incidence of post-operation infection; for impromptu bowel cleansing and sterilization; for routine bladder irrigations; for trichomonas, monilia and other infections of the vaginal tract; for many ENT cases; and for oral surgery, etc.

Clorpactin WCS-90 should not be used for surgery involving tumours or cancer. *Clorpactin XCB* is suggested for these cases.

Further information may be obtained from the sole South African distributors:

Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg. *Telephone*: 23-0314.

TRESCATYL

Maybaker (S.A.) (Pty.) Ltd. announce the introduction of a new product *Trescatyl* brand ethionamide.

Trescatyl is indicated for the treatment of pulmonary tuberculosis in patients for whom 2 or more of the standard anti-tuberculosis drugs are unsuitable because of the presence of drug-resistant organisms or other contra-indications.

Where possible, sensitivity of the patient's organisms to available drugs and to ethionamide should be determined before treatment is started.

Trescatyl is given orally in a dosage of 0.5 to 1 gramme daily in 2, 3 or 4 portions and it must be administered in conjunction with the most suitable of the other available anti-tuberculosis drugs.

Trescatyl is available in tablets of 250 mg. in containers of 250.

REVIEWS OF BOOKS

PAEDIATRIC PRESCRIBER

Paediatric Prescriber. By Pincus Catzel, M.B., B.Ch. (Rand), M.R.C.P. (Edin.), D.C.H., R.C.P. & S. (Eng.). (1959. Pp. 223 + Index. 15s.). Oxford: Blackwell Scientific Publications.

The author has excelled in compiling a comprehensive, detailed tabulation of almost every drug which can be used in almost any situation. The book is concise and filled with masses of useful information which is most accessible. The chapters on poisons and antidotes, infants' food, immunization and immunological products and fluid therapy are excellent and fully detailed. The chapter on therapy in skin diseases is approached from the standpoint of the therapeutic agent and the diagnosis. The methods suggested are simple and most efficacious.

The author stresses in his introduction that all drugs are potentially toxic and should not be prescribed until their actions, uses, side effects and contra-indications have been studied. In the foreword Sheldon stresses these points too; also that no rule-of-thumb formula can be devised for correct dosage in infants and children, e.g. he quotes the large doses of drugs which are used in epilepsy which have no relation to height, weight or age. A serious fault in this book is what appears to be the author's lack of experience with many drugs, such as the comprehensive list of drugs used for hypertension, the antihistamines, the tranquillizers and the various endocrine preparations. Among the hypertensive drugs, a number of those used in adult therapy are listed. In actual fact they have hardly ever been tried for infants and children. A tested drug of value is magnesium sulphate, which is mentioned, but by the intramuscular route, whereas the intravenous administration of a 1% solution, given very carefully, is undoubtedly the drug of choice in hypertensive crises.

The indications for, or benefit of antihistamines as a whole, have (in the reviewer's opinion) been grossly exaggerated; yet 7 are detailed. The author states that local applications are relatively ineffective and may cause sensitization. Why then does he recommend a number of them? Similarly, local applications of antibiotics are ineffective. They may lead to sensitization and, even worse, the organisms may become drug resistant; yet again preparations are listed.

The doubtful value of the tranquillizers is beautifully illustrated by the author's excellent quotation:

> 'Optimism is the greatest Analgesic
> Hope is the most certain Tranquillizer.'

Why not leave it at that?

Several methods for calculating dosage are given in the *Appendix*, but one which is undoubtedly most useful is discarded as being 'too cumbersome.' This is the application of dosage based on surface area, which deserves greater consideration as it has been shown that the levels of most drugs closely follow this formula. It can be applied not only to drug dosage but also to fluid and dietary allowances. The hypothesis is rational because blood and plasma volume, cardiac output, renal blood flow and glomerular filtration are clearly standardized on the basis of surface area. Drugs administered on the plan show calculated levels in a number of instances. (*See* Butler, A. M. and Riche, R. H., *New England Journal of Medicine*, 1960, **262**, 903). The surface area in relation to height and weight is read off a normogram or a weight chart. All drugs are calculated on this basis in Nelson's *Textbook of Pediatrics*, 7th ed., the Bible of every paediatrician.

The indiscriminate use of endocrine preparations in children cannot be condemned too strongly. In

this book a plan of therapy for amenorrhoea in children is given. It is better to do nothing in such cases and give Nature a chance. Dehydroepiandrosterone, a real tongue-twister, is quoted as 'being used in cases of constitutional psychological inadequacy in adolescents, characterised by inferiority feelings, apathy and lack of confidence.' Other literature recommends a Carnegie course for the same symptoms.

It is stated that Troxidone (Tridione) should not be used as a first line of attack for *petit mal*. This drug is specific for this condition. Alevaire is described as a mucolytic agent which is very 'popular.' This drug has been shown under controlled experiments to be of doubtful value. In view of the well-known dangers of aspirin in infants, is the insertion of Acetyl Salicylic Acid Mixture for Infants (BPC) justified? The author correctly mentions that vitamin K in the premature may cause hyperbilirubinaemia, a most serious condition. He then suggests that it can be given to the mother before delivery—an equally dangerous procedure. Recently, too, it has been shown that chloromycetin (given in large doses to the premature infant) often causes severe jaundice or even sudden collapse and death, which is not mentioned. This is an object lesson in the danger of drugs which have been used for many years in millions of instances and only recently found to have severe toxic effects. Another drug of which this is true is Gantrisan in premature infants; there may be many others.

The author (an undoubted authority on fibrocystic disease of the lung) lists 2 preparations of pancreatic extract. The reader would have been assisted by the expression of a definite view on their value. The author states that Tincture of Belladonna may be useful (in a dosage of 10 minims) for enuresis, but says that side effects may be marked and the dosage should immediately be reduced. The reviewer, on numerous occasions, has given a dosage up to 35 or 40 minims with no ill effects.

The book mentions that aminophyllin should not be given with ephedrine, yet several such preparations are on the market and no ill effects have been observed from their use.

The antimicrobial agents are discussed in a special section. The author stresses 3 points:

Avoidance of indiscriminate and unnecessary use of drugs;

Wrong choice of drug; and

Inadequate dosage.

These points are praiseworthy and deserve great emphasis. The good work is nullified by detailing all the antimicrobial agents on the market and unintentionally encouraging the practitioner to use them. This encouragement is also manifest by detailing the agents under specific diseases, giving them increased status by acknowledging that the information is modified from *Martindale*. Recently the reviewer investigated a big series of upper respiratory infections treated with different antimicrobial agents and found that the results were far better with the sulphonamides or penicillin than any of 4 'mycins.' This is a most useful point, as it shows that in large-scale treatment of cases, the expense can be greatly reduced. In cases of influenzal Meningitis, e.g. over the years the best results have been attributed to combined therapy with a sulphonamide, streptomycin and chloromycetin; and in the last 2 years a tetracycline has supposedly lowered the mortality rate still further. In the last year it has been shown that the results with chloromycetin alone are equally good, if not better. The moral of the story is that in general practice the use of most of the recorded agents is not only unnecessary, but may also be harmful. All these agents should be carefully evaluated by large institutions of repute.

The public deserves protection, *not because these drugs are dangerous* but because, in most instances, they are *unnecessary, ill-chosen, inadequately given,* and (perhaps of equal importance) *expensive.*

A great deal of the reviewer's criticism has been made for two reasons. Firstly, this book is to be published simultaneously in England, Canada and America and will therefore be read by a great number of practitioners. Secondly, when it is revised, all doubtful and little-used preparations should be removed.

Finally, the author should have stressed the various agents which he has personally found of great value. If he had then proceeded to list the other agents in the Appendix under the heading 'not proven,' a great deal of criticism would have fallen away. This would have encouraged greater caution on the part of the medical practitioner and would have protected the patient, who is the one who counts.

This book represents a great deal of painstaking effort on the part of the author and if the criticisms are noted, it will prove a most valuable addition to the practitioner's reference library.

DAVIDSON'S PRACTICE OF MEDICINE

The Principles and Practice of Medicine. By Sir Stanley Davidson, B.A. Cantab., M.D., F.R.C.P. Edin., F.R.C.P. Lond., M.D., Oslo, F.R.S. Edin. (1960. Pp. 1083 + Index. With 73 Figs. 35s.). Edinburgh & London: E. & S. Livingstone Ltd.

It is not surprising that the demand for this remarkably utilitarian manual has become so phenomenal, as evidenced by this fifth edition only 2 years after its predecessor, with a reprint in the year between. The *Principles and Practice of Medicine,* written for students and doctors, has fulfilled its functions so admirably that 5 editions and 4 large reprints have appeared in its short life of 8 years.

Inevitably the pressing need to accommodate new material has led to an increase in the size of the volume—by 45 pages. But this has been kept down to a modest minimum by eliminating redundant and old material.

A striking feature of the presentation is the critical, scientific approach exemplified very typically in the discussion of the medical management of peptic ulcer, where a common-sense appraisal of diet and drugs distinguishes the advice given and puts in perspective much of the mythological ritual which embroiders this subject (pp. 764–766).

The volume represents the admirable teaching and practice of the Department of Medicine of the University of Edinburgh, an institution which many South African medical practitioners are happy to regard as their *alma mater.* Those who have a different academic loyalty will nevertheless find in the lucid pages and the pertinent illustrations of this book a succinct and helpful guide to the problems of actual practice. It is particularly well-designed to meet the requirements of the medical student and the general practitioner.

CELL AND TISSUE CULTURE

Cell and Tissue Culture. By John Paul, M.B., Ch.B., Ph.D., M.R.C.P.Ed. 1959. (Pp. 256 + Index. With 40 Figs.). Edinburgh and London: E. & S. Livingstone Ltd.

In the past 10 years tissue cultures have become as important for diagnostic work as any media in a routine laboratory. The vast amount of literature that has accumulated on the subject is bewildering to the beginner. Hence Dr. Paul's excellent book will be greatly welcomed. It is based on the *Tissue Culture Association Summer Course,* Denver, Colorado, which is directed by Dr. Paul of the University of Glasgow.

The book is divided into 4 parts. *Part I* deals with cell structure, basic embryology, the metabolism of cells and their nutritional requirements plus 3 invaluable, detailed chapters on media.

Part II deals with the choice and preparation of apparatus whilst *Parts III* and *IV* describe in detail individual techniques, especially the preparation of cell cultures.

The book is intended for students learing the techniques. It is an up-to-date account of techniques and applications of modern tissue culture, which are clearly and concisely presented. For the experienced worker it may be too elementary, but even he can derive much useful information. Each chapter has a very good bibliography quoting only kev references.

Of particular value are the numerous simple drawings conveying a great deal of information.

HYPNOSIS FOR GENERAL PRACTITIONERS

Hypnotism for Medical and Dental Practitioners. By A. A. Mason, M.B., B.S. (1960. Pp. 219 + Index. 30s.). London: Secker & Warburg.

Dr. Mason starts his book with the sentence: 'In the last few years, a great number of books on hypotism have appeared and, in presenting yet another, I have to ask myself what purpose it serves?'

How right to ask oneself this question—but how bold to answer this oneself! The answer is simply that indeed very little purpose is served. No general practitioner would dare write a treatize on surgery or obstetrics and gynaecology. But alas, psychology and psychiatry are playing fields open to any one who has a ball to kick. The nature of the hynotic state, of the therapy involving hypnosis, plus the implications of this unique relationship, are highly complex and specialized phenomena. It is no coincidence, then, that the basic textbooks in hypnosis have been written by psychiatrists and psychologists.

The opening chapters on the technique of hynotic induction and the levels of hypnotic trance are competently handled. The next chapter, on the nature of the hypnotic state, is only superficially dealt with. None of the theories is discussed in any detail and it is surprising to find no mention made of the more recent theories based on the neuro-physiological advances of Penfield and Jasper. The chapters on actual treatment were the most exasperating. A quotation from page 85 gives us the central core of the author's thesis:

'Basically, the treatment of psycho-somatic disorders by hypnosis is the direct suggestion, in the hypnotic state, that the lesion will go.'

This view can be dangerous. There is little doubt that symptoms can be but surface expressions of deep fundamental conflicts and may fulfil an important function in maintaining the psycho-biological equilibrium of the individual.

Descriptions of lecture demonstrations, in which subjects are made to hallucinate the presence of tigers (page 124), are unnecessarily theatrical for a book of this nature.

The chapter on *Dentistry* by K. Dawson Watts is extremely well written. The need for psychiatric advice when treating thumb-sucking is a point well made. The final chapter on *Hypnosis in Obstetrics,* by S. D. Perchard, is excellent. It is intelligently planned and deals with each phase of the delivery carefully.

The last two chapters save this from being a rather inconsequential book.

CONGENITAL HEART DISEASE

An Introduction to Congenital Heart Disease. By Leo Schamroth, M.B., B.Ch. (Rand), M.R.C.P.E., F.R.F.P.S. and Fay Segal, M.D. (Rand). (1960. Pp. 112 + Index. With 82 Figs. 22s.). Oxford: Blackwell Scientific Publications.

The authors have set out to produce a book designed as a guide to congenital heart disease for the student and the practitioner. This explains the lack of detail in their description of various forms of congenital heart disease.

The text is concise and pertinent, and the illustrations are excellent. The inclusion of brief discussions on embryology is praiseworthy.

By and large, the book would appear to fulfil its purpose. It is a pity, however, that more detail is not devoted to a general discussion of physical signs and their interpretation, as the student and the practitioner are required to elicit and interpret physical signs in all cases.

The authors discuss 12 different congenital anomalies, including the rare anomaly of Ebstein and tricuspid atresia, but omit to discuss the more common anomaly of congenital aortic stenosis.

These mild criticisms notwithstanding, the book fills a role as an introductory manual to congenital heart disease.

LOCOMOTOR DISORDERS

Diagnosis in Locomotor Disorders. By Kenneth Stone, D.M. (Oxon.), M.R.C.P. (1960. Pp. 218 + Index. With 53 Figs. 25s.). London, New York, Toronto and Cape Town: Oxford University Press.

This short book is in the form of a series of articles on symptoms or signs of any diseases of the nervous system, bones, joints and soft tissues which can affect locomotion. The articles are arranged alphabetically so that the student can turn to the presenting symptom and find a differential diagnosis with a few facts about each illness. The X-ray reproductions are good and demonstrate the abnormalities well.

It is difficult to conceive the class of reader for whom this book was really intended. Most symptoms are dealt with in a manner which is too superficial for the practitioner, even for a busy casualty officer who needs to refresh his memory on some point. Little detail is included, so that in each of the differential diagnoses the user will have to refer to a conventional textbook. This result is, of course, inevitable in the attempt to keep a large number of facts within the compass of a volume of this size.